Message from Placer County Health & Human Services and the Placer/Nevada County Medical Society

Dear Placer County Physician,

Placer County Health and Human Services and the Placer/Nevada County Medical Society are pleased to help you understand the physician's role in a biological or chemical terrorist attack. We are the caregivers for the community. To provide effective care, reassurance and counseling, you must have information.

This "Primer" is not a legal or scientific document, but a straightforward and brief summary of what we all need to know. The Infectious Disease specialists at the local, state, and national level culled the information from many sources. We have made every attempt to accurately reflect best practices and make this as useful as possible. Yet we have also documented this as Version 1.0 in anticipation of finding meaningful ways in which we might improve upon it's usefulness based upon your feedback. Please contact Placer County Health and Human Services Communicable Disease Control at (530) 889-7141 with any suggestions you might have as you familiarize yourself with this document.

Thank you for taking the time to read this and to prepare for what we hope never happens. All of us operate on a daily basis under the premise if you hear hoof beats it must be a horse, in our current situation it's important that we all consider that it just might be a zebra. Our patients and the community need to know that we are ready!

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Introduction

Recent events have re-alerted us to potential threats of Bioterrorism. Bioterrorism is defined by the CDC as "The intentional or threatened use of viruses, bacteria, fungi, toxins from living organisms, or other chemicals, to produce death or disease in humans, animals or plants."

This document is designed to be an overview – a primer – on Bioterrorism in Placer County. It provides a brief summary of clinically relevant information dealing with the recognition, reporting, treatment and infection control/public health implications of several of the potential biological and chemical agents that could be utilized. It is being sent to every physician in Placer County.

It is not designed to be a technical reference document. We have included phone numbers on Page 2, and Web sites at the end of the document, for you to get more detailed information.

Responding appropriately to Bioterrorism is a three step process: Identify, Report, and Refer:

- Identify – we want you, as a result of this document, to be aware of the symptoms of Bioterrorism, to know the appropriate tests, and to know some of the differential diagnoses.
- Report – we want you to be able to contact the correct agencies and be able to initiate the cascade of pre-programmed responses by public agencies.
- Refer – we want you to be able to refer victims of Bioterrorism to those who know how to treat them and to refer the media to those who know the most about this subject.

DO's - What do we want you to do?

- Read the material.
  - If you are so inclined, check out the web sites for additional reading or research.
- Be extra vigilant with your patients.
- Share this information with your patients – allay their fears.
- Understand the probabilities associated with Bioterrorism and the limits of the Bioterrorism agents.
- Refer the media to the experts.
- If in doubt, ask County Public Health– THEY HAVE THE ANSWERS!

DON'Ts – What do we not want you to do?

- Prescribe antibiotics inappropriately.
- Stockpile antibiotics.
- Recommend the use of gas masks.

Overview of Bioterrorism and Antibiotics

The Centers for Disease Control and Prevention (CDC), the California Department of Health Services, the Placer County Health & Human Services, the Placer/Nevada County Medical Society, the Infectious Disease Society of America, and the Infectious Diseases Association of California have all stated that you SHOULD NOT PRESCRIBE ANTIBIOTICS OR VACCINES to prevent potential Bioterrorism related infections.

No single antibiotic will protect against all potential agents. Many agents could be used in a Bioterrorist event, including bacteria, viruses, chemical or biological toxins. The necessary measures to prevent or minimize morbidity and mortality are specific for each agent.

The duration of protection conferred by antibiotics is short, and the duration needed for ongoing protection is undefined (essentially limitless in the absence of a discrete event). If and when there is a Bioterrorism event, clinical and public health evaluation will determine who would benefit from antibiotic administration. Indiscriminate antibiotic use needlessly diminishes existing supplies, increases drug resistance and may lead to adverse events.

Availability of antibiotics and vaccines will be most critical at the actual sites where Bioterrorism has occurred. CDC has a plan in place to distribute antibiotics and/or vaccines to the specific locations where they are needed through the National Pharmaceutical Stockpile (NPS) Program. CDC has made a commitment to deploy supplies relevant to a given Bioterrorism event within 12 hours via a series of regional NPS warehouses. Recent deployments have demonstrated the capacity to perform as promised.

Individual medical providers do not have access to either anthrax or smallpox vaccine at this time.

It is possible that agents used for a Bioterrorism event will have been engineered to be resistant to the established therapies and perhaps even to vaccines.

Overview of Bioterrorism Response

All physicians should be on the alert for unusual cases or large clusters of cases of illnesses that resemble the “flu” which could be the first evidence of Bioterrorism.

The occurrence of even a single case of an infection that is not endemic in Placer County should be reported to the Health Department.

Individual Physicians’ actions (in the case of a suspect Bioterrorism event NOT in their office):

- Keep their offices open.
- Take the Bioagent Infection Control Measures specified on pages 3&4, given the Bioterrorism agent.
- Contact the Placer County public health staff at (530-889-7141) if you feel you have a patient related to the incident.
- If you have a television in your office, turn it on for public health alerts.

Hospitals actions:

- Be prepared to isolate infected individuals, as appropriate.
- Targeted chemoprophylaxis and vaccination will constitute the best available responses.

County Public Health actions:

- Activate the County Emergency Operations Center (EOC)
- Initiate prompt investigation of original case.
- Contact identification, interview and investigation.
- Conduct specimen collection, examination, and verification of results.
- Collaborate with State of California and CDC as indicated.
- Notify FBI, State, CDC and the local medical community as appropriate.
- Conduct heightened surveillance for similar illness.
- Determine need for treatment of contacts, health professionals.
- Manage all public information releases out of EOC.
- Mobilize additional resources at regional, state and federal levels as needed.
- Maintain constant contact with reporting Doctor and Facility.

Telephone Numbers

Call First: Placer County Health and Human Services Communicable Disease Control: Monday-Friday - (530) 889-7141, Weekends, after hours - (530) 889-7119

General Information on Bioterrorism

The most likely agents are:

- Bacillus anthracis (anthrax).
- Yersinia pestis (plague); pulmonary syndrome.
- Francisella tularensis (tularemia); pulmonary syndrome.
- Variola (smallpox).
- Clostridium botulinum (botulism).
- Viral hemorrhagic fevers: Ebola, Marburg, Lassa, etc…

The most common syndromes are:

- Acute respiratory distress with fever.
- Influenza-like illness.
- Gastrointestinal illnesses.
- Skin lesions.
- Acute onset neuromuscular symptoms/signs.

Clues to unnatural occurrences of infections are:

- An unusual increase in numbers of patients presenting with a similar syndrome.
- A large number of fatal cases.
- Clusters of an illness from a single locale or temporally related.
- Any infection that is non-endemic in Placer County.
- Common infections occurring during unusual seasons (i.e. influenza in Placer County in summertime).
- Increase in sick or dead animals.
- Intelligence information.

Bioagents versus the Flu

- As several of the bioagents may produce febrile illnesses with respiratory symptoms/signs that could be confused with influenza, during the annual influenza season in Placer County (December - March) the clinician should consider performing specific, diagnostic tests for the presence of influenza virus or antigen.
- Several rapid diagnostic tests are commercially available and can be performed on sputum samples.
- Viral isolation is also available and may assist in the management of these patients and others in the community (i.e. use of specific anti-influenza medications and vaccine optimization).
- Negative rapid tests do not exclude influenza as a diagnosis, but a positive test will reassure you and the patient.
- Remember to give Flu vaccines, where indicated by the CDC guidelines and do not initiate an “early” schedule.

Bioagent-Specific Infection Control Measures

- Anthrax Standard Precautions.
  - Pulmonary infection is NOT transmitted person to person.
  - Cutaneous infection can be transmitted by drainage.
- Smallpox Airborne Precautions (like tuberculosis).
- Plague Droplet Precautions (standard masks for 72 hours after Rx).
- Botulism Standard Precautions.
- TularemiaStandard Precautions.
- Hemorrhagic Fever Standard Precautions, Airborne Precautions, Droplet Precautions and Contact Precautions to avoid exposures due to excessive hemoptysis, or hemetemesis.
  - Treat blood stained material as infectious.

Bioagent Infection Control Measures

Standard Precautions

- Standard precautions are employed in the care of ALL patients, under ALL circumstances.
- Wash hands after patient contact.
- Wear gloves when touching blood, body fluids, secretions, excretions and contaminated items.
- Wear a mask and eye protection, or a face shield during procedures likely to generate splashes or sprays of blood, body fluids, secretions or excretions.
- Handle used patient-care equipment and linen in a manner that prevents the transfer of microorganisms to people or equipment.
- Use care when handling sharps and use a mouthpiece or other ventilation device as an alternative to mouth-to-mouth resuscitation when practical.

Airborne Precautions

- Standard Precautions plus:
- Place the patient in a private room that has monitored negative air pressure, a minimum of six air changes/hour, and appropriate filtration of air before it is discharged from the room.
- Wear respiratory protection when entering the room.
- Limit movement and transport of the patient. Place a mask on the patient if they need to be moved.
- Conventional diseases requiring Airborne Precautions: measles, varicella, and pulmonary tuberculosis.
- **Biothreat diseases requiring Airborne Precautions: smallpox, viral hemorrhagic fevers**.

Droplet Precautions

- Standard Precautions plus:
- Place the patient in a private room or cohort them with someone with the same infection. If not feasible, maintain at least 3 feet between patients.
- Wear a mask when working within 3 feet of the patient.
- Limit movement and transport of the patient. Place a mask on the patient if they need to be moved.
- Conventional diseases requiring Droplet Precautions: invasive haemophilus influenzae and meningococcal disease, drug-resistant pneumococcal disease, diphtheria, pertussis, mycoplasma, gabhs, influenza, mumps, rubella, parvovirus.
- **Biothreat diseases requiring Droplet Precautions: pneumonic plague, viral hemorrhagic fevers.**

Contact Precautions

- Standard Precautions plus:
- Place the patient in a private room or cohort them with someone with the same infection if possible.
- Wear gloves when entering the room. Change gloves after contact with infective material.
- Wear a gown when entering the room if contact with patient is anticipated or if the patient has diarrhea, a colostomy or wound drainage not covered by a dressing.
- Limit the movement or transport of the patient from the room.
- Ensure that patient-care items, bedside equipment, and frequently touched surfaces receive daily cleaning.
- Dedicate use of noncritical patient-care equipment (such as stethoscopes) to a single patient, or cohort of patients with the same pathogen. If not feasible, adequate disinfection between patients is necessary.
- Conventional diseases requiring Contact Precautions: MRSA, VRE, clostridium difficile, RSV, parainfluenza, enteroviruses, enteric infections in the incontinent host, skin infections (SSSS, HSV, impetigo, lice, scabies), hemorrhagic conjunctivitis.
- **Biothreat Diseases requiring Contact Precautions: viral hemorrhagic fevers**

Bacterial Agents of Bioterrorism

Anthrax

- Description: a spore forming gram-positive rod, which can cause disease by inhalation, inoculation, or ingestion of spores, which, upon reversion to regular bacterial forms, produce potent “edema” and “lethal” toxins.
- The pneumonic, or inhalational, form starts 1-6 days after exposure with, fever, myalgias cough and fatigue, which after a brief improvement, progress to an abrupt respiratory distress and shock. There are no specific physical findings, but the chest x-ray may show a widened mediastinum, with or without effusion, but mostly without, infiltrates, because the disease is primarily a mediastinitis. Fifty percent have associated meningitis.
- Diagnosis: widened mediastinum on CXR, Gram-positive rods may be found on gram stains of CSF or buffy coats, and positive blood cultures later in the illness.
- Treatment: IV doxycycline or quinolones (supernormal doses) for 4 weeks, plus vaccination.
- Prophylaxis: avoid inhalation of contaminated material, doxycycline or Ciprofloxacin x 8 weeks plus vaccination (3 doses).
- Pediatrics: doxycycline or penicillin, or cipro (see guidelines)
- Isolation: Standard. No person-to-person transmission of inhalation anthrax.
- Inoculation (cutaneous) anthrax may appear in conjunction with inhalation cases. Local tissue destruction results in the formation of a black eschar or ulcer with (+/-severe) surrounding edema. Some develop septicemia.
- Gastrointestinal anthrax occurs when large numbers of spores are ingested. It may present with nausea and vomiting, abdominal pain, bloody diarrhea +/- ascites, which progresses to an acute abdomen. The toxins destroy the mesenteric lymph nodes and the circulation to the small bowel.

Plague

- Description: *Yersinia pestis* is a gram-negative rod, which causes disease in two forms.
- The pneumonic form begins 2-3 days after inhalation of an aerosol, either from an infected patient or from a bioterrorist aerosol source, with sudden onset of myalgias, high fevers, headache and cough with bloody sputum. Within one day it progresses to a fulminant pneumonia with dyspnea, stridor, cyanosis, septic shock with DIC and hepatocellular damage. The chest x-ray has consolidation /infiltrates. Six percent have associated meningitis.
- The bubonic form would probably not be used as a bioagent.
- Diagnosis: cultures and gram stains of blood, sputum, CSF and lymph node aspirates. Immunoassays available.
- Treatment: gentamicin, doxycycline or chloramphenicol (for meningitis).
- Prophylaxis: doxycycline.
- Isolation: mandatory for at least the first 48 hours of treatment.
- Pediatric: doxycycline or trimethoprim/sulfa for prophylaxis but gentamicin or chloramphenicol for treatment.

Tularemia

- Description: Tularemia is caused by *Francisella tularensis*, a small, fastidious Gram-negative bacillus. Human infections can occur via aerosols, contaminated food or water, from arthropod bites, or through skin exposure.
- The incubation period can be as short as 24 hours, but can be up to 14 days or longer. Sporadic cases of tularemia occur in most parts of the USA, and tularemia is endemic among small animals in California. Although the infectious dose of F. tularensis is very low, there is no evidence for person-to-person transmission of infection.
- Each route of infection produces a different clinical picture. Clinical or radiographic features cannot differentiate tularemia pneumonia from other serious bacterial pneumonias. The usual result of inhalation is pneumonia with hilar adenopathy and/or pleural effusions in about 1/3 of cases. High fever, chills, rigors, sore throat, myalgias (elevated CPK in some) and a non-productive cough are common. There may be pulse-temperature dissociation. Untreated, the mortality of tularemia pneumonia may reach 50%. Ingestion is more likely to cause exudative tonsillitis and supporative cervical adenitis.
- Diagnosis is difficult because the bacteria are fastidious and grow slowly, they may not grow out of sputum on standard blood agar, or the laboratory may not recognize them. Rapid diagnostic tests are not available. Blood and pleural fluid cultures may be positive. Aspirates of enlarged lymph nodes will also yield the pathogen. Serology can be used for retrospective diagnosis. A four-fold titer increase or a titer above 1:160 is diagnostic, but this usually takes 10-14 days to develop.

- Treatment is with parenteral gentamicin 5mg/kg qd, or doxycycline 100 mg, or chloramphenicol 15mg/kg q 6h, or erythromycin 500 mg q. 8h. Because this organism can be drug-resistant, in vitro susceptibility testing should guide subsequent treatment. Doxycycline or fluoroquinolones can be used for prophylaxis in people who were likely exposed but not yet ill. There is no available vaccine. Contaminated surfaces can be cleaned with 10% bleach and then wiped with 70% alcohol. Cloths and skin can be washed with soap and water.

Viral Agents of Bioterrorism

General Discussion

- Viral agents proposed for use as biologic weapons include Smallpox (variola virus), Venezuelan Equine Encephalitis Virus, and the multiple agents causing viral hemorrhagic fevers, typified by Ebola.
- General characteristics of these viruses include:
  - Initial presentation with non-specific flu-like symptoms.
  - Pathogenesis secondary to direct cytopathic effect, immune-complex deposition, or other processes often resulting in vascular injury and end-organ failure.
  - Vaccination most effective prophylaxis but few vaccines generally available for proposed agents.
  - Few antiviral agents have proven efficacy or are available.

Smallpox – Variola virus

- Declared eradicated 1980 by WHO, known stockpiles of virus still remain at the CDC in Atlanta and at the Institute for Viral preparations in Moscow and possibly at other sites in the world. In the USA, civilian vaccination programs ended in the early 1980's while the military stopped in 1989.
- Virus is spread by aerosol with incubation period averaging ~12 days (7-19days).
- Clinical symptoms begin with abrupt onset of malaise, fevers, rigors, headache, emesis, backache, and delirium (15%) followed 2-3 days later by onset of rash on face, hands, forearms, and legs then spreading centrally with lesions progressing from macules to papules to pustular vesicles. Lesions typically are in the same stage of development.
- Patients are highly infectious during the initial respiratory phase and remain so until all eschars are off. Mortality is about 30% in unvaccinated population. Mortality is lower in vaccinated individuals, but no civilians have maximal protection because vaccination ceased 30 years ago.
- Characteristics differentiating the Rashes of Variola and Varicella:

Variola	Varicella
Centrifugal	Centripetal
Lesions all at the same stage	Lesions in various stages
Slow evolution	Rapid evolution
Deep lesions: circular and regular Scarring: severe	Superficial lesions: oval or irregular Scaring: mild

- Clinical diagnosis of Varicella virus infection (i.e. chickenpox) is adequate if the clinical presentation is typical. Atypical or unusually severe cases of Varicella should prompt consideration of laboratory testing to confirm the diagnosis of Varicella; the exclusion of Varicella, either via rapid diagnostic testing for Varicella antigen or viral culture should suggest the possibility of a pox virus infection or another alternate diagnoses.
- Treatment: Cidofovir and other antivirals but none are proven effective. Isolation: Airborne.
- Vaccination within 3 days of exposure will prevent disease and within 5 days life-saving. CDC has 12 – 14 million doses of vaccine. Oral vaccine in development.

Equine Encephalitis Viruses

- Togaviridae, all can be infectious by aerosol, easily produced and stable. VEE studied as a weapon by USA. Susceptibility is high (90-100%) with ~ 100% of those infected develop acute disease.
- Incubation period of 1-6 days followed by acute febrile illness with malaise, myalgias, fevers, rigors, severe headache, and photophobia x 24-72 hours followed by nausea, emesis, cough, sore throat, and diarrhea. 0.5-4% will develop encephalitis with altered mental status.
- Diagnosis on clinical and epidemiological grounds. Exam is non-specific. Lab often with leukopenia and lymphopenia, increased AST, and lymphocytic pleocytosis in CSF. Confirmation provided by viral isolation (throat, serum, CSF), serology (IgM available) and PCR.
- Treatment is supportive, mortality < 1% (increased at extremes of life), vaccine is experimental. Isolation: Airborne.

Viral Hemorrhagic Fevers

- Caused by various RNA viruses, usually with an animal reservoir. All are potentially infectious by aerosol with high morbidity and mortality.
  - Arenaviridae: Lassa, Argentine, Bolivian, Venezuelan, and Brazilian
  - Bunyaridae: Rift Valley Fever, Congo-Crimean, Hantaviruses
  - Filoviradae: Ebola, Marburg
  - Flaviviridae: Yellow Fever
- All hemorrhagic fever viruses can cause capillary leak syndromes.
- Incubation period 5-10 days (Filoviradae) followed by malaise, fever, myalgias, prostration, conjunctival injection, petechiae, ecchymoses, shock, diffuse hemorrhage, neurologic dysfunction and pulmonary collapse. Increased LFT's and renal dysfunction poor prognosis.
- Diagnosis based on clinical and epidemiologic parameters. Definitive diagnosis: serology, PCR, and viral isolation.
- Treatment is largely supportive, avoiding ASA/antiplatelet drugs, Ribavirin (Lassa, CCHF, HFRS, and RVF). Vaccine available for Yellow Fever, Argentine, Bolivian, and Rift Valley Fever. Isolation = Airborne.

Influenza Virus

- As several of the bioagents may produce febrile, respiratory symptoms/signs, during the annual influenza season in Placer County (December - March), the clinician should consider performing specific, diagnostic tests for the presence of influenza virus or antigen. Several rapid diagnostic tests are commercially available and can be performed on sputum samples. Viral isolation is also available and may assist in the management of these patients and others in the community (i.e. use of specific anti-influenza medications and vaccine optimization).

Biological Toxins of Bioterrorism

General Discussion

Biological toxins are products of living organisms, which produce illness or death after aerosol inhalation or ingestion. Substances are non-volatile and not likely to produce secondary person-person exposure - use Standard Precautions.

Botulinum Toxin

- (Types A-G) Most poisonous substance known. Botulinum toxin prevents release of acetylcholine at presynaptic nerve terminal and blocks nerve transmission. Aerosolized or food borne, typically presents 12-72 hours after exposure
- Symptoms
  - 4D's - diplopia, dysarthria, dysphonia, dysphagia.
  - Ptosis, mydriasis, generalized weakness, dizziness, dry mouth and throat, blurred vision, respiratory failure.
  - Naturally occurring food-borne botulism more prone to preceding abdominal cramps, nausea, vomiting and diarrhea secondary to other bacterial metabolites in food.
- Clinical Diagnosis
  - Symmetrical descending flaccid paralysis with prominent bulbar palsies,
  - Afebrile
  - Clear sensorium.
- Differential Diagnosis
  - Guillain-Barre,
  - Myasthenia gravis,
  - Tick paralysis,
  - Conversion reaction
- Action
  - Call public health department,
  - Draw at least 30cc blood (red top),
  - Sample feces, gastric secretions or vomitus.
  - Refrigerate samples and submit any suspect food.
  - Send list of patient's medications with samples.
  - Mouse neutralization assay can confirm diagnosis.
- Decontamination
  - If suspected aerosol release, breathe through clothing.
  - Intact skin is impermeable, but wash skin with 0.1% hypochlorite or soap/water.
  - Persistence of aerosolized toxin is dependent on atmospheric conditions and is usually inactivated by 2days.
  - In food, the toxin is inactivated by heat.
- Treatment
  - Botulinum antitoxin (to be used at first signs of illness) will minimize severity, but not reverse existent paralysis. Paralysis can persist for weeks to months. Respiratory support, nutritional and fluid management, treatment of complications
  - Botulinum Toxoid Vaccine is an investigational agent for individuals at high risk and is not effective in post exposure prophylaxis.

Staphylococcal Enterotoxin B (SEB)

- Symptoms
  - 2-12 hours after exposure. Fever (for 2-5days), chills, headache, myalgia, nonproductive cough (up to 4weeks).
  - May have SOB, retrosternal chest pain, nausea, vomiting, diarrhea, conjunctival injection, hypotension, CXR usually normal, but can have atelectasis, pulmonary edema.
  - Incapacitation for up to 2 weeks is usual, but rarely can progress to sepsis/death.
- Diagnosis - clinical; nonspecific labs, elevated WBC, ESR.
- Differential Diagnosis - influenza, adenovirus, mycoplasma.
- Action - Draw acute and convalescent sera, urine sample for public health lab.
- Decontamination - hypochlorite 0.5% or 10-15min soap/water.
- Treatment - supportive, respiratory support, fluid management.

Ricin

- Derived from castor bean, inhibits protein synthesis which results in cell death.
- Symptoms - (in 4-8 hours) weakness, fever, cough, hypothermia.
  - Inhalation - severe respiratory symptoms from necrosis and edema, hypoxia with respiratory failure in 36 -72 hours.
  - Ingestion - Nausea, vomiting, diarrhea, GI hemorrhage, vascular collapse, death. May cause DIC, multiple organ failure
- Diagnosis - Lab nonspecific, Serum ELISA available.
- Differential Diagnosis - SEB, Q Fever, tularemia, plague, phosgene. Collect serum samples.
- Decontamination - hypochlorite 0.5% solution, and/or soap/water.
- Treatment - supportive, O2, hydration. If ingestion, gastric lavage, superactivated charcoal followed by cathartics.

Trichothecene

- Mycotoxins, T2. Fungal toxin- stable to heat and UV. Inhibits protein and nucleic acid synthesis affecting rapidly proliferating tissues. If aerosolized, it appears as yellow droplets - "yellow rain" – which can adhere to and penetrate skin, be inhaled and swallowed.
- Symptoms - onset minutes-4 hours- skin pain, pruritis, redness, vesicles, epidermal slough, eye irritation, nose throat pain, sneezing, wheezing, cough, dyspnea, chest pain, hemoptysis, abdominal pain, vomiting, bloody diarrhea. Bone marrow suppression can lead to diffuse hemorrhage. If severe, prostration, ataxia, collapse, shock and death in hours to days.
- Diagnosis - urine, blood, tissue samples for liquid chromatography-mass spectrometry.
- Decontamination - remove and isolate clothing, irrigate eyes with saline; wash with soap/water.
- Treatment - symptomatic/ supportive. If ingested, superactivated charcoal. No antidote.

Chemical Agents of Terrorism

Nerve Agents

- Description
  - Organophosphates bind and inactivate acetylcholinesterase. colorless, nearly odorless
  - Sarin (GB)
  - Tabun (GA)
  - Soman (GD)
  - VX - clear ,
- Diagnosis - acute onset cholinergic crisis. Sarin may cause death in 1-10 minutes
- Symptoms
  - Respiratory - irritation to mucous membranes, cough, airway constriction and increased secretions
  - Neuromuscular -twitch, weakness, paralysis, respiratory failure
  - Autonomic -blurred vision, pinpoint pupils, drooling, sweating, tearing, nausea, vomiting, abdominal pain, diarrhea
  - Central Nervous System -slurred speech, confusion, headache, convulsions, respiratory arrest
  - Cardiovascular - tachycardia, bradycardia, arrhythmia, heart block
- Decontamination - move victim to fresh air, remove and isolate clothing, wash skin/eyes with water/saline. 0.5% hypochlorite to skin if possible
- Treatment
  - Oxygen/respiratory support, suction secretions. Rush to healthcare facility
  - Atropine (antagonizes muscarinic effects) 2 mg deep IM injection, IV, or ET, Repeat q5-10min until secretions are drying and decreased airway resistance (to max 20 mg.) Infant (0.5mg IM or 0.02mg/kg), child 2- 10(1 mg IM), elderly lmg) This will not have any effect on pupils or skeletal muscle.
  - Pralidoxime chloride (2 PAM chloride)-helps nicotinic neuromuscular sites. Separates nerve agent from AChE, (but once "aging" has occurred, nerve agent is permanently attached to AChE, 2PAM will no longer be effective) 1g IV over 20-30 min., may repeat in 1 hour (child< 20kg--15mg/kg,child >20kg - 600mg IM autoinjector, elderly 7.5mg/kg) Use Phentolamine for 2PAM induced hypertension (adult 5mg IV, child 1mg IV)
  - Diazepam - 10mg IM (2-5mg IV) Child 1mo-5yr- 0.2-0.5mg/kg;child >5y - 1 mg IV
  - Supportive care for weeks may be necessary

Vesicants

- General Effects
  - Cell damage, tissue necrosis, toxic byproducts, metabolic acidosis, secondary infections, pulmonary insufficiency
- Mustard
  - HD H- latent period hours- erythema and blisters on skin, irritation, conjunctivitis, mild upper respiratory sx to marked airway damage. Also GI effects, nausea and vomiting, bone marrow suppression
  - Wash with water and dilute hypochlorite
  - Topical antibiotics, pulmonary support, analgesics
- Lewisite
  - L- immediate pain, skin and mucous membrane irritation, erythema, blisters skin, eye and airway
  - Wash water/hypochlorite. British Anti-Lewisite antidote (BAL)

Industrial Chemicals

- Phosgene - CG- odor of fresh cut grass, hay.
  - Damages alveolar-capillary membrane. Toxic to lungs by inhalation- immediate burning, eye and airway damage, SOB, cough; Pulmonary edema can develop in 2-12 hours
  - Treatment- Fresh air, wash with water, symptomatic management of lesions, pulmonary care, careful fluid replacement, absolute rest
- Cyanide
  - Inhibits the body's ability to transfer oxygen and CO2 at the capillaries. Agent is volatile
  - Symptoms - seizures, respiratory, and cardiac arrest.
  - Decontamination - remove clothing; wash with water
  - Treatment- antidotes: intravenous sodium nitrite and sodium thiosulfate.
  - Supportive oxygen and correction of acidosis
- Riot Control Agents (Mace®, pepper spray)
  - Symptoms - burning pain skin, mucous membranes and eyes
  - Treatment - flush with water, soap and water or dilute sodium bicarbonate solution. (Hypochlorite should NOT be used)
  - Effects are self-limited, unless underlying asthma/emphysema or hysteria from fear of nerve agent exposure

Overview of Vaccines for Bioagents

Anthrax

- The anthrax vaccine was developed in the 1950s and is a strain producing a protective antibody response in 7 days. Doses are required at 0, 2, 4, 6, 12 and 18 months with annual boosters. The United States military first started mass vaccinating troops for the Gulf war in 1991. The military still routinely vaccinates personnel against anthrax. The anthrax vaccine is only recommended for people between 18 and 65.
- There is a great deal of debate about the safety and efficacy of the anthrax vaccine in the setting of intentional aerosol exposure. There is no solid data on anthrax vaccine safety, especially in large numbers of people, and the incidence of systemic adverse reactions appears to be about 0.006-.5%. There have been no randomized trials done in humans for intentional exposure.

- Although minor local reactions are common (about 30%), the best data suggest that systemic reactions are rare (0.06 - 0.5%). Unfortunately, the data from recent military vaccination programs has been incomplete. It's always possible that more adverse reactions will come to light when a vaccine like this is given to large numbers of people but, based on the existing data, it appears to be pretty safe (Moran, GJ. Biological Terrorism Part I and II. Emergency Medicine, 2000).
- Although no gold-standard double-blind, placebo controlled human efficacy trials have been conducted, a single-blind, placebo controlled trial using the less potent form of the vaccine was conducted in goat hair mill workers in New Hampshire from 1955-59. The vaccine conferred statistically significant reduction in the incidence of anthrax overall (cutaneous plus inhalational) and suggested a reduction in the incidence of inhalational anthrax, but the numbers of cases of inhalational disease were too small to attain statistical significance. In addition, trials on non-human primates and guinea pigs have shown that the vaccine is effective against fatal disease due to infection by the aerosol route. (Friedlander, A. M., P. R. Pittman, et al. (1999). "Anthrax Vaccine: Evidence for Safety and Efficacy Against Inhalational Anthrax." Journal of the American Medical Association 282:2104-6.)
- In the setting of a known or strongly suspected anthrax exposure, the potential benefit of the vaccine would likely exceed the risk. The risk/benefit balance for pre-exposure vaccination for large numbers of people is debatable, since the probability of exposure is very low for most (Moran, GJ. Biological Terrorism Part I and II. Emergency Medicine, 2000).

Smallpox

- The existing vaccine may prevent or ameliorate illness if given with in 3-4 days of exposure. Passive immunization is capable through vaccinia immune globulin if given within the first 24 hours of exposure. There are approximately 5 to 10 million doses of the small pox vaccine in the United States, however no distribution program currently exists. (Gordon, S. M. (1999). "The Threat of Bioterrorism: A Reason to Learn More About Anthrax and Smallpox." Cleveland Clinic Journal of Medicine 66(10): 592-600.)
- The United States has contracted with OraVax Inc (Cambridge, MA) who is subcontracting with Bio-Reliance (Washington, DC) to begin developing more vaccines. The initial production of 40 million doses is not expected to be complete until 2004 (www.LocalBusiness.com).

Viral Hemorrhagic Fevers

- An investigational new drug (IND) vaccine is available for yellow fever as well as for Argentine hemorrhagic fever (AHF) that may also protect for Bolivian hemorrhagic fever (BHF). There are also two vaccines for Rift Valley fever (RVF) designed by the military. The first vaccine requires 3 boosters and then is effective for 20 years. The second is a live attenuated strain that is still being tested. (Franz, D.R, e. a. (1997). "Clinical Recognition and Management of Patients Exposed to Biological Warfare Agents." Journal of the American Medical Association 278(5): 399-411.)

Plague

- A USA licensed formaldehyde-killed whole bacilli vaccine was discontinued in 1999 because it was only effective against bubonic plague. Research is currently underway for a vaccine to protect against pneumonic plague. (Inglesby, T. V. e. a. (2000). "Plague as a Biological Weapon." Journal of the American Medical Association 283(17): 228-90.)

Tularemia

- There is an attenuated live tularemia vaccine currently available in the United States as an IND. (Franz, D.R, e. a. (1997). "Clinical Recognition and Management of Patients Exposed to Biological Warfare Agents." Journal of the American Medical Association 278(5): 399-411.)

Botulism

- There is an IND vaccine for botulism currently available in the United States. (Franz, D.R, e. a. (1997). "Clinical Recognition and Management of Patients Exposed to Biological Warfare Agents." Journal of the American Medical Association 278(5): 399-411.)

Viral Encephalitis

- Immunizations are available for Venezuelan equine encephalitis (VEE), western equine encephalitis (WEE), and eastern equine encephalitis (EEE) in the United States but may require multiple injections and are poorly immunogenic. Adequate immunization against encephalitis may require polyvalent vaccines. (Franz, D.R, e. a. (1997). "Clinical Recognition and Management of Patients Exposed to Biological Warfare Agents." Journal of the American Medical Association 278(5): 399-411.)

Key Websites

www.idac.org - Infectious Disease Association of California. **THE HOTLINK "BIOTERRORISM DOCUMENTS" WILL PROVIDE YOU WITH NEARLY ALL OF THE IMPORTANT DETAILED DOCUMENTS!**

www.bt.cdc.gov - The most complete site for information on biological terrorism.

www.hopkins-biodefense.org

www.medepi.org/sfdph/bt/syndromes/index.html -The San Francisco Department of Public Health Department with syndromic approach to potential biological agents with differential diagnoses and pictures.

www.usamriid.army.mil/education/bluebook.html - The US Army Medical Research Institute of Infectious Diseases "Medical Management of Biological Casualties Handbook"

http://www.nbc-med.org/ie40/Default.html - Nuclear, Biological and Chemical Diseases website: (Including textbook of military medicine and management of biologic casualties.

http://www.dhs.ca.gov/ps/dcdc/bt/index.htm -CA State Health Dept., Division of Communicable Disease Control

http://www.dhs.ca.gov/Bioterrorism%20Headline/Revised%20BT%20Response%20master%20document.pdf - California Hospital Bioterrrorism Response Planning Guide DRAFT

http://www.ph.ucla.edu/cphdr/bioterrorism has an excellent FAQ section as well as a good PowerPoint presentation

Ten Critical Steps for Handling Possible Bioterrorist Events

1 - Maintain an index of suspicion.	In an otherwise healthy population, some associations are very suggestive, especially when seen in clusters, high numbers, or unusual presentations. *"Clustered" Symptoms* *Potential Bioagents* Hemoptysis Plague Flaccid Paralysis Botulism Purpura Viral Hemorrhagic Fevers (VHF) Wide mediastinum Anthrax Centripetal rash Smallpox
2 - Protect yourself and your patients	Use appropriate personal protection equipment (PPE). Prophylaxis: vaccines, if available; or antibiotics, if risks are known
3 - Adequately assess the patient	Review and assess the patient's history. Also, ask: • Are others ill? • Were there any unusual events? • Was there an uncontrolled food source or other environmental factor? • Was there vector exposure? • Has the patient been traveling? • What is the patient's immunization record? Perform a physical examination with special attention to the respiratory system, nervous system, skin condition, and hematologic and vascular status
4 - Decontaminate as appropriate	Do not use bleach on exposed people. Soap, water and shampoo are perfectly adequate for all biological and most chemical agents. **ALL COTHES IN A TERRORIST EVENT ARE EVIDENCE AND SHOULD BE BAGGED PRESENTED TO LAW ENFORCEMENT**
5 - Establish a diagnosis.	Think clinically and epidemiologically; always send specimens as appropriate coordinating with public health. *Symptom (individuals)* *Possible Diagnosis* Pulmonary Tularemia, plague, staph enterotoxin B (SEB) Neuromuscular Botulism, Venezuelan equine encephalitis (VEE) Bleeding/purpura VHF, ricin, plague (late) Rash (various types) VHF, T2 mycotoxin, smallpox, plague Flu-like symptoms Varies Immediate Symptoms (large numbers) Possible Diagnosis Pulmonary SEB, mustard, Lewisite, phosgene, cyanide Neurologic Nerve gases, cyanide Delayed Symptoms (large numbers) Possible Diagnosis

	Pulmonary Biologic agents, mustard, phosgene Neurologic Botulism, VEE, other encephalitis
6 - Render prompt treatment.	**A**irway, **B**reathing, **C**irculation.
7 - Provide good infection control	• Gown, gloves, mask and hand washing, and eyewear if necessary, are sufficient. • Recommended isolation precautions for biologic agents include: • Standard Precautions - For all individuals/patients • Contact Precautions - Viral Hemorrhagic Fevers • Droplet Precautions - Pneumonic Plague and Tularemia • Airborne Precautions - Smallpox
8 - Alert the proper authorities.	CALL FIRST: Placer County Health and Human Services, Communicable Disease Control: Monday-Friday - (530) 889-7141, Weekends, after hours - (530) 889-7119 FBI & CDC will be contacted by County*: FBI (858) 565-1255 , Center for Disease Control (CDC) – (800) 311-3435*
9 - Assist in the epidemiologic investigations	Steps in an epidemiologic investigation so as to determine who may be at risk. • COMMUNICATE • Count cases; • Relate to the at-risk population; • Make comparisons; • Develop hypotheses; • Test hypotheses; • Make inferences; • Conduct studies; • Interpret and evaluate; • COMMUNICATE.
10- Know and spread this information	

Chemical Agents Reference Chart

CHEMICAL	SYMPTOMS	TREATMENT
Nerve Agents Tabun Sarin Soman VX	**S**alivation. **L**acrimation. **U**rination. **D**efecation. **G**astric - **E**mptying. Pinpoint pupils (everything looks dark). Seizures.	Atropine – initial dose 2 mg. Additional doses until symptoms resolved (will not reverse miosis). Pralidoxime Chloride – 1 gram IV over 20–30 minutes. Benzodiazepines – for seizure control or to prevent seizures in severely intoxicated patients.
Cyanides Hydrogen Cyanide Cyanogen Chloride	Non-specific: anxiety, hyperventilation, respiratory distress. Cherry-red skin, though classic, is seldom seen. Lactic acidosis and increased concentration of venous oxygen.	**Cyanide Antidote Kit** Amyl nitrite ampule – first aid until IV established. Crush and place inside mask of BVM; 15 seconds of inhalation, then 15 second break; repeat until IV established. Sodium nitrite – 300 mg over 2–4 minutes. Sodium thiosulfate – 12.5 g over 5 minutes.
Vesicants Mustard Lewisite	Redness and blisters. Inhalation injury may result in respiratory distress. Leukopenia to pancytopenia.	Topical antibiotics. Systemic analgesics. Fluid balance (do not overhydrate; not a thermal burn). Bronchodilators and steroids for pulmonary symptoms, **only** if Lewisite is the poison, then BAL is the antidote.
Pulmonary Intoxicants Chlorine Phosgene	Delayed onset of non-cardiogenic pulmonary edema.	Treat hypotension with fluid; no diuretics. Ventilate with PEEP. Bronchodilators.
Riot Control Agents: Pepper Spray, Mace, Tear Gas	Ear, nose, mouth and eye irritation.	Irrigate. Treat bronchospasm with bronchodilators and steroids, as needed.

Biological Agents Reference Chart

AGENT	DETECTION	TREATMENT
Anthrax	I: 1–6 d. FLS. Possible widened mediastinum. Gram stain (gram-positive rod) of blood and blood culture (late).	TBI: treatment may be delayed 24 h. until cultures from incident site available. PEP (only if instructed by govt. officials): ciprofloxacin or doxycycline po x 8 wks. Severe cases: ciprofloxacin, doxycycline, or penicillin IV.
Cholera	I: 4 h–5 d. Severe gastroenteritis with "rice water" diarrhea.	Oral rehydration with WHO solution or IV hydration. Tetracycline, doxycycline (dosage as below or 300 mg one time) po for 3 d. Ciprofloxacin or norfloxacin po for 3 d. if resistant strains.
Plague	I: 2-3 d. FLS. CXR: patchy infiltrates or consolidation. Gram stain of lymph node aspirate, sputum, or CSF (gram negative, non-spore forming rods).	**Isolation.** PEP: doxycycline or ciprofloxacin for 7 days Symptomatic: gentamicin or doxycycline IV for 10–14 days. Meningitis: chloramphenicol.
Tularemia	I: 2-10 d. FLS.	Gentamicin for 10–14 d.
Q Fever	I: 10-40 d. FLS.	Most cases self-limited. Tetracycline or doxycycline po for 5–7 d.
Smallpox	I: 7-17 (avg. 12) d. FLS. Later erythematous rash that progresses to pustular vesicles. Electron or light microscopy of pustular scrapings. PCR.	**Isolation.** PEP: vaccinia vaccine scarification and vaccinia immune globulin IM.
Viral Encephalitides	I: 1-6 d. FLS. Immunoassay.	Supportive.
Viral Hemorrhagic Fevers	I: 4-21 d. FLS. Easy bleeding and petechiae. Enzyme immunoassay.	**Isolation**. Supportive care. Some respond to ribavirin.
Botulism	I: 1-5 d. Descending bulbar, muscular and respiratory weakness.	Supportive. PEP: toxoid. Symptomatic: anti-toxin.
Staphylococcus Enterotoxin B	I: 3-12 h. FLS.	Supportive.
Ricin	I: 18-24 h. FLS, pulmonary edema, and severe respiratory distress.	Supportive.
T-2 Mycotoxins	I: 2-4 h. Skin, respiratory and GI symptoms.	Supportive.

Abbreviations: CSF: cerebro-spinal fluid. **CXR**: chest x-ray. **d**: days. **h**: hours. **FLS**: flu-like symptoms. **GI**: gastro-intestinal. **I**: incubation period. **PCR**: polymerase chain reaction. **PEP**: post-exposure prophylaxis. **TBI**: threatened biologic incident. **WHO**: World Health Organization.
Dosages: **Chloramphenicol**: 50-75 mg/kg/d, divided q 6 hrs. **Ciprofloxacin**: po: 500 mg q 12 h.; IV: 400 mg q 8-12 h. **Doxycycline**: po: 100 mg q 12 hrs; IV: 200 mg initially then 100 mg q 12 h. **Erythromycin**: po: 500 mg q 6 h. **Gentamicin**: 3-5 mg/kg/d. **Norfloxacin**: po: 400 mg. **Penicillin**: IV: 2 million units q 2 h. **Tetracycline**: po: 500 mg q 6 h. **Streptomycin**: IM: 15 mg/kg, BID. **Vaccinia immune globulin**: IM: 0.6 mL/kg.
WHO solution: 3.5 g NaCl, 2.5 g $NaHCO_3$, 1.5 g KCl and 20 g of glucose per liter of water.

Compiled by Richard N. Bradley, MD, Asst. Med. Dir., Houston Fire Dept. EMS Division.

DIFFERENTIAL DIAGNOSIS CHART BY SYNDROME

Syndrome	Differential Diagnosis	Bioterrorism Threat Disease Description	Initial laboratory & other diagnostic test results	Immediate public health & infection control actions
Acute Respiratory Distress with Fever	Dissecting aortic aneurysm, inhalational anthrax, pulmonary embolism	**Inhalational Anthrax:** Abrupt onset of fever; chest pain; respiratory distress without radiographic findings of pneumonia; no history of trauma or chronic disease; progression to shock and death within 24-36 hours	Chest x-ray with widened mediastinum; gram-positive bacilli in sputa or blood; definitive testing available through public health laboratory network.	Call Placer County Public Health. Alert laboratory to possibility of anthrax. Standard precautions.
Acute Respiratory Distress with Fever	Community acquired pneumonia, Hantavirus Pulmonary Syndrome, meningococcemia, pneumonic plague, rickettsiosis	**Pneumonic Plague**: Apparent severe community-acquired pneumonia but with hemoptysis, cyanosis, gastrointestinal symptoms, shock	Gram-negative bacilli or coccobacilli in sputa, blood or lymph node; safety-pin appearance with Wright or Giemsa stain; definitive testing available through public health laboratory network.	Call Placer County Public Health. In addition to standard precautions, droplet precautions with a regular surgical mask. Call hospital infection control and Local Health Department. Ask family members/close contacts of patient to stay at the hospital (if already present) for public health interview/chemoprophylaxis; get detailed address and phone number information. Alert laboratory of possibility of plague.
Acute Respiratory Distress with Fever	Plague, Q fever, Staphylococcal enterotoxin B, phosgene, tularemia	**Ricin (aerosolized):** Acute onset of fever, chest pain and cough, progressing to respiratory distress and hypoxemia; not improved with antibiotics; death in 36-72 hours	Chest x-ray with pulmonary edema. Consult with Local Health Department regarding specimen collection and diagnostic testing procedures.	Call Placer County Public Health. Standard precautions.
Acute Respiratory Distress with Fever	Influenza, adenovirus, mycoplasma	**Staphylococcal enterotoxin B**: Acute onset of fever, chills, headache, nonproductive cough and myalgia (influenza-like illness) with a NORMAL chest x-ray.	Primarily clinical diagnosis. Consult with Local Health Department regarding specimen collection and diagnostic testing procedures.	Call Placer County Public Health. Standard precautions.
Acute Rash with Fever	Varicella, disseminated herpes zoster, vaccinia, monkeypox, cowpox	**Smallpox:** Papular rash with fever that begins on the face and extremities and uniformly progresses to vesicles and pustules; headache, vomiting, back pain, and delirium common	Clinical with laboratory confirmation; vaccinated, gowned and gloved person obtains specimens (scabs or swabs of vesicular or pustular fluid). Call public health immediately before obtaining specimen; definitive testing available through public health laboratory network.	Call Placer County Public Health. Call hospital infection control immediately. In addition to standard precautions, contact and airborne precautions required. Ask family members/close contacts of patient to stay at the hospital (if already present) for public health interview and vaccination; get detailed address and phone number information.
Acute Rash with Fever	Meningococcemia, malaria, typhus, leptospirosis, borreliosis, thrombotic thrombocytopenic purpura (TTP), Hemolytic Uremic Syndrome (HUS)	**Viral Hemorrhagic Fever (e.g., Ebola):** Fever with mucous membrane bleeding, petechiae, throbocytopenia and hypotension in a patient without underlying malignancy	Definitive testing available through public health laboratory network--call public health immediately.	Call Placer County Public Health. Call Hospital infection control. Standard and contact precautions. Ask family members/close contacts of patient to stay at the hospital (if already present) for public health interview and follow-up; get detailed address and phone number information.

Neurologic Syndromes	Guillain-Barre Syndrome; myasthenia gravis; midbrain stroke; tick paralysis; Mg++ intoxication; organophosphate, carbon monoxide, paralytic shellfish, or belladonna-like alkaloid poisoning; polio; Eaton-Lambert myasthenic syndrome	**Botulism:** Acute bilateral descending flaccid paralysis beginning with cranial nerve palsies	CSF protein normal; EMG with repetitive nerve stimulation shows augmentation of muscle action potential; toxin assays of serum, feces, or gastric aspirate available through public health laboratory network.	Call Placer County Public Health Request botulinum antitoxin from local/state health department. Standard precautions.
Neurologic Syndromes	Herpes simplex, post-infectious	**Encephalitis** (Venezuelan, Eastern, Western): Encephalopathy with fever and seizures and/or focal neurologic deficits.	Serologic testing available through public health laboratory network.	Call Placer County Public Health. Standard precautions.
Influenza-like Illness	Numerous diseases, including Q Fever	**Brucellosis:** Irregular fever, chills, malaise, headache, weight loss, profound weakness and fatigue. Arthralgias, sacroiliitis, paravertebral abscesses. Anorexia, nausea, vomiting, diarrhea, hepatosplenomegaly. May have cough and pleuritic chest pain.	Tiny, slow-growing, faintly-staining, gram-negative coccobacilli in blood or bone marrow culture. Leukocyte count normal or low. Anemia, thrombocytopenia possible. CXR nonspecific: normal, bronchopneumonia, abscesses, single or miliary nodules, enlarged hilar nodes, effusions. Serologic testing and culture available through public health laboratory network.	Call Placer County Public Health. Notify laboratory if brucellosis suspected--microbiological testing should be done in a biological safety cabinet to prevent lab-acquired infection. Standard precautions.
Influenza-like Illness	Numerous diseases, including Q Fever	T**ularemia** (Typhoidal, Pneumonic): Fever, chills, rigors, headache, myalgias, coryza, sore throat initially; followed by weakness, anorexia, weight loss. Substernal discomfort, dry cough if pneumonic disease.	Small, faintly-staining, slow-growing, gram-negative coccobacillus in smears or cultures of sputum, blood. CXR may show infiltrate, hilar adenopathy, effusion. Definitive testing available through public health laboratory network.	Call Placer County Public Health. Notify laboratory if tularemia suspected--microbiological testing should be done in a biological safety cabinet to prevent lab-acquired infection. Standard precautions.
Blistering Syndromes	Mustard agents, Staphylococcal enterotoxin B	**T2 Mycotoxin:** Abrupt onset of mucocutaneous and airway irritation including skin (pain and blistering), eye (pain and tearing), gastrointestinal (bleeding, vomiting, and diarrhea), and airway (dyspnea and cough)	Consult with Local Health Department regarding specimen collection and diagnostic testing procedures.	Call Placer County Public Health. Unlike other biological agents or biotoxins, trichothecene mycotoxins are dermally active and patients exposed to them should be decontaminated as soon as possible with soap and copious amounts of water.

Recognition of Illness Associated with the Intentional Release of a Biologic Agent

On September 11, 2001, following the terrorist incidents in New York City and Washington, D.C., CDC recommended heightened surveillance for any unusual disease occurrence or increased numbers of illnesses that might be associated with the terrorist attacks. Subsequently, cases of anthrax in Florida and New York City have demonstrated the risks associated with intentional release of biologic agents (1). This report provides guidance for health-care providers and public health personnel about recognizing illnesses or patterns of illness that might be associated with intentional release of biologic agents.

Health-Care Providers

Health-care providers should be alert to illness patterns and diagnostic clues that might indicate an unusual infectious disease outbreak associated with intentional release of a biologic agent and should report any clusters or findings to their local or state health department. The covert release of a biologic agent may not have an immediate impact because of the delay between exposure and illness onset, and outbreaks associated with intentional releases might closely resemble naturally occurring outbreaks. Indications of intentional release of a biologic agent include 1) an unusual temporal or geographic clustering of illness (e.g., persons who attended the same public event or gathering) or patients presenting with clinical signs and symptoms that suggest an infectious disease outbreak (e.g., ≥2 patients presenting with an unexplained febrile illness associated with sepsis, pneumonia, respiratory failure, or rash or a botulism-like syndrome with flaccid muscle paralysis, especially if occurring in otherwise healthy persons); 2) an unusual age distribution for common diseases (e.g., an increase in what appears to be a chickenpox-like illness among adult patients, but which might be smallpox); and 3) a large number of cases of acute flaccid paralysis with prominent bulbar palsies, suggestive of a release of *botulinum* toxin.

CDC defines three categories of biologic agents with potential to be used as weapons, based on ease of dissemination or transmission, potential for major public health impact (e.g., high mortality), potential for public panic and social disruption, and requirements for public health preparedness (2). Agents of highest concern are *Bacillus anthracis* (anthrax), *Yersinia pestis* (plague), variola major (smallpox), *Clostridium botulinum* toxin (botulism), *Francisella tularensis* (tularemia), filoviruses (Ebola hemorrhagic fever, Marburg hemorrhagic fever); and arenaviruses (Lassa [Lassa fever], Junin [Argentine hemorrhagic fever], and related viruses). The following summarizes the clinical features of these agents (*3--6*).

Anthrax. A nonspecific prodrome (i.e., fever, dyspnea, cough, and chest discomfort) follows inhalation of infectious spores. Approximately 2--4 days after initial symptoms, sometimes after a brief period of improvement, respiratory failure and hemodynamic collapse ensue. Inhalational anthrax also might include thoracic edema and a widened mediastinum on chest radiograph. Gram-positive bacilli can grow on blood culture, usually 2--3 days after onset of illness. Cutaneous anthrax follows deposition of the organism onto the skin, occurring particularly on exposed areas of the hands, arms, or face. An area of local edema becomes a pruritic macule or papule, which enlarges and ulcerates after 1--2 days. Small, 1--3 mm vesicles may surround the ulcer. A painless, depressed, black eschar usually with surrounding local edema subsequently develops. The syndrome also may include lymphangitis and painful lymphadenopathy.

Plague. Clinical features of pneumonic plague include fever, cough with muco-purulent sputum (gram-negative rods may be seen on gram stain), hemoptysis, and chest pain. A chest radiograph will show evidence of bronchopneumonia.

Botulism. Clinical features include symmetric cranial neuropathies (i.e., drooping eyelids, weakened jaw clench, and difficulty swallowing or speaking), blurred vision or diplopia, symmetric descending weakness in a proximal to distal pattern, and respiratory dysfunction from respiratory muscle paralysis or upper airway obstruction without sensory deficits. Inhalational botulism would have a similar clinical presentation as foodborne botulism; however, the gastrointestinal symptoms that accompany foodborne botulism may be absent.

Smallpox (variola). The acute clinical symptoms of smallpox resemble other acute viral illnesses, such as influenza, beginning with a 2--4 day nonspecific prodrome of fever and myalgias before rash onset. Several clinical features can help clinicians differentiate varicella (chickenpox) from smallpox. The rash of varicella is most prominent on the trunk and develops in successive groups of lesions over several days, resulting in lesions in various stages of development and resolution. In comparison, the vesicular/pustular rash of smallpox is typically most prominent on the face and extremities, and lesions develop at the same time.

Inhalational tularemia. Inhalation of *F. tularensis* causes an abrupt onset of an acute, nonspecific febrile illness

beginning 3--5 days after exposure, with pleuropneumonitis developing in a substantial proportion of cases during subsequent days (*7*).

Hemorrhagic fever (such as would be caused by Ebola or Marburg viruses). After an incubation period of usually 5--10 days (range: 2--19 days), illness is characterized by abrupt onset of fever, myalgia, and headache. Other signs and symptoms include nausea and vomiting, abdominal pain, diarrhea, chest pain, cough, and pharyngitis. A maculopapular rash, prominent on the trunk, develops in most patients approximately 5 days after onset of illness. Bleeding manifestations, such as petechiae, ecchymoses, and hemorrhages, occur as the disease progresses (*8*).

Clinical Laboratory Personnel

Although unidentified gram-positive bacilli growing on agar may be considered as contaminants and discarded, CDC recommends that these bacilli be treated as a "finding" when they occur in a suspicious clinical setting (e.g., febrile illness in a previously healthy person). The laboratory should attempt to characterize the organism, such as motility testing, inhibition by penicillin, absence of hemolysis on sheep blood agar, and further biochemical testing or species determination.

An unusually high number of samples, particularly from the same biologic medium (e.g., blood and stool cultures), may alert laboratory personnel to an outbreak. In addition, central laboratories that receive clinical specimens from several sources should be alert to increases in demand or unusual requests for culturing (e.g., uncommon biologic specimens such as cerebrospinal fluid or pulmonary aspirates).

When collecting or handling clinical specimens, laboratory personnel should 1) use Biological Safety Level II (BSL-2) or Level III (BSL-3) facilities and practices when working with clinical samples considered potentially infectious; 2) handle all specimens in a BSL-2 laminar flow hood with protective eyewear (e.g., safety glasses or eye shields), use closed-front laboratory coats with cuffed sleeves, and stretch the gloves over the cuffed sleeves; 3) avoid any activity that places persons at risk for infectious exposure, especially activities that might create aerosols or droplet dispersal; 4) decontaminate laboratory benches after each use and dispose of supplies and equipment in proper receptacles; 5) avoid touching mucosal surfaces with their hands (gloved or ungloved), and never eat or drink in the laboratory; and 6) remove and reverse their gloves before leaving the laboratory and dispose of them in a biohazard container, and wash their hands and remove their laboratory coat.

When a laboratory is unable to identify an organism in a clinical specimen, it should be sent to a laboratory where the agent can be characterized, such as the state public health laboratory or, in some large metropolitan areas, the local health department laboratory. Any clinical specimens suspected to contain variola (smallpox) should be reported to local and state health authorities and then transported to CDC. All variola diagnostics should be conducted at CDC laboratories. Clinical laboratories should report any clusters or findings that could indicate intentional release of a biologic agent to their state and local health departments.

Infection-Control Professionals

Heightened awareness by infection-control professionals (ICPs) facilitates recognition of the release of a biologic agent. ICPs are involved with many aspects of hospital operations and several departments and with counterparts in other hospitals. As a result, ICPs may recognize changing patterns or clusters in a hospital or in a community that might otherwise go unrecognized.

ICPs should ensure that hospitals have current telephone numbers for notification of both internal (ICPs, epidemiologists, infectious diseases specialists, administrators, and public affairs officials) and external (state and local health departments, Federal Bureau of Investigation field office, and CDC Emergency Response office) contacts and that they are distributed to the appropriate personnel (*9*). ICPs should work with clinical microbiology laboratories, on- or off-site, that receive specimens for testing from their facility to ensure that cultures from suspicious cases are evaluated appropriately.

State Health Departments

State health departments should implement plans for educating and reminding health-care providers about how to recognize unusual illnesses that might indicate intentional release of a biologic agent. Strategies for responding to potential bioterrorism include 1) providing information or reminders to health-care providers and clinical laboratories about how to report events to the appropriate public health authorities; 2) implementing a 24-hour-a-day, 7-day-a-week capacity to receive and act on any positive report of events that suggest intentional release of a biologic agent; 3) investigating immediately any report of a cluster of illnesses or other event that suggests an intentional release of a biologic agent and requesting CDC's assistance when necessary; 4) implementing a plan, including

accessing the Laboratory Response Network for Bioterrorism, to collect and transport specimens and to store them appropriately before laboratory analysis; and 5) reporting immediately to CDC if the results of an investigation suggest release of a biologic agent.

Reported by: National Center for Infectious Diseases; Epidemiology Program Office; Public Health Practice Program Office; Office of the Director, CDC.

Editorial Note:

Health-care providers, clinical laboratory personnel, infection control professionals, and health departments play critical and complementary roles in recognizing and responding to illnesses caused by intentional release of biologic agents. The syndrome descriptions, epidemiologic clues, and laboratory recommendations in this report provide basic guidance that can be implemented immediately to improve recognition of these events.

After the terrorist attacks of September 11, state and local health departments initiated various activities to improve surveillance and response, ranging from enhancing communications (between state and local health departments and between public health agencies and health-care providers) to conducting special surveillance projects. These special projects have included active surveillance for changes in the number of hospital admissions, emergency department visits, and occurrence of specific syndromes. Activities in bioterrorism preparedness and emerging infections over the past few years have better positioned public health agencies to detect and respond to the intentional release of a biologic agent. Immediate review of these activities to identify the most useful and practical approaches will help refine syndrome surveillance efforts in various clinical situations.

Information about clinical diagnosis and management can be found elsewhere (1--*9*). Additional information about responding to bioterrorism is available from CDC at <*http://www.bt.cdc.gov*>; the U.S. Army Medical Research Institute of Infectious Diseases at <*http://www.usamriid.army.mil/education/bluebook.html*>; the Association for Infection Control Practitioners at <*http://www.apic.org*>; and the Johns Hopkins Center for Civilian Biodefense at <*http://www.hopkins-biodefense.org*>.

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